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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/820,099	03/27/2001	Jan G.J. van de Winkel	MXI-170	2545

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EXAMINER
HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
1642	10

DATE MAILED: 10/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/820,099	VAN DE WINKEL, JAN G.J.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *13-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,6* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-12 in Paper No. 9 is acknowledged.

2. Claims 13-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9.

3. Claims 1-12 are under examination.

Specification

4. The disclosure is objected to because of the following informalities:

a. The first line of the specification should be updated to indicate that the instant application claims priority to provisional application 60/192,727.

b. The Brief Description of the Drawings needs to recite "Figure 1A-D", "Figure 2A-D", "Figure A-H".

Appropriate correction is required.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

6. Claims 1-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Shen et al (WO 98/23646, published 6/98, IDS #4) as evidenced by Monteiro et al (J. Exp. Med 171:597-613, 1990) and the specification.

The claims recite a method for eliminating a target cell or antigen from the circulatory system of a subject comprising administering a complex comprising an antibody that binds FcαRI expressed on Kupffer cells linked to a second portion comprises an antibody that binds a cancer target cell or antigen, wherein the first portion of the complex binds a site of FcαR that is distinct from the binding site for IgA, further claimed is the target antigen is a bacteria, virus, fungus, the antibody is humanized, further the method comprises administration of GM-CSF, further administration is by intravenous.

Shen et al teach bifunctional antibodies comprising an antibody that binds FcαRI and a bacteria (see page 22) or cancer cell or antigen (see page 19-20) thereof wherein the binding is not inhibited by endogenous IgA (see page 4, lines 28-29), further is a method for eliminating cells or antigen in a subject by administration of the bispecific

antibody to a subject (see page 28-29) and the method further comprises adding GM-CSf which enhances the number or activity of Fcα receptors (see page 28) and the method comprises administration intravenous (see page 29, line 35) and the antibodies can be humanized (see page 11, lines 28-page 12). As evidenced by Monteiro et al (and the specification at page 1, lines 6-8) there is only a single class of IgA Fc receptor, Fcα RI, therefore since the antibody binds to Fcα RI, it would be inherent that the antibody would bind to Fcα RI expressed on Kupffer cells and adding cytokine would increase the expression of the Fcα RI on Kupffer cells.

7. Claims 1-7, 11-12 are rejected under 35 U.S.C. 102(e) as being anticipated by van de Winkel (U.S. Patent 6,111,166, filed 6/27/97) and as evidenced by Monteiro et al (J. Exp Med 171:597-613, 1990) and the specification.

The claims have been described supra.

Van de Winkel teach bifunctional antibodies comprising an antibody that binds FcαRI and a virus, bacteria, or fungus (see column 9, lines 58-60) or cancer cell or antigen (see column 9, lines 1-7) thereof wherein the binding is not inhibited by endogenous IgA (see column 7, lines 40-48), further is a method for eliminating cells or antigen in a subject by administration of the bispecific antibody to a subject (see Example V) and the method comprises administration intravenous (see column 12) and the antibodies can be humanized (see column 6, lines 64-66). As evidenced by Monteiro et al and the specification on page 1, lines 6-8 there is only a single class of

IgA Fc receptor, Fcα RI, therefore since the antibody binds to Fcα RI, it would be inherent that the antibody would bind to Fcα RI expressed on Kupffer cells.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over van de Winkel (U.S. Patent 6,111,166, filed 6/27/97) as evidenced by Monteiro et al (J. Exp. Med. 171:597-613, 1990) and the specification, as applied to claim1-7 and 11-12 above, and further in view of Morton et al (Critical Reviews in Immunology 16:423, 1996, IDS #6).

The claims have been described supra.

Van de Winkel has been described supra. Van de Winkel also teach the Fcα RI has an affinity that is increased upon exposure to GM-CSF (see column 5, lines 54-37). Van de Winkel does not teach administration of GM-CSF to a subject which increases the expression of Fcα RI of Kupffer cells. This deficiency is made up for by the teachings of Morton et al.

Morton et al teach expression of Fcα RI can be upregulated by many factors and cytokines, specifically TNF-α (see page 429).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have added a cytokine to the method of van de Winkel in view of the teachings of Morton et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have added a cytokine to the method of van de Winkel in view of the teachings of Morton et al because van de Winkel teach the affinity of the FcαRI is increased upon adding cytokines. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have added a cytokine to the method of van de Winkel in view of the teachings of Morton et al because Morton et al teach that the expression of the FcαRI is upregulated in many cell lines that express FcαRI. Because the expression is upregulated in many cells by cytokines, it would be obvious that one of the cytokines would increase the expression in the Kupffer cells.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879

LARRY HELMS
PATENT EXAMINER